A Novel Biodegradable Poly(urethane ester) Synthesized from Poly(3-hydroxybutyrate) Segments

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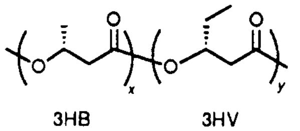
Introduction. A wide variety of microorganisms produce poly(3-hydroxybutyrate) (P(3HB)) as a carbon and energy supply.[1] Recently, Imperial Chemical Industries (ICI) has developed a controlled fermentation process for the production of optically active copolyesters of (*R*)-3-hydroxybutyrate and (*R*)-3-hydroxyvalerate (P(3HB-*co*-3HV), 1).[2] In these types of polyesters, the optically active (*R*)-3-hydroxyalkanoic acids play an important role in their biodegradability, biocompatibility, and other physical properties.[1,3] However, this fermentation technique is expensive and inefficient. The synthesis of such high molecular weight polymers by ring opening of (*R*)- or (*S*)-β-butyrolactone has also shown to be costly,[4] and the direct condensation polymerization of (*R*)-3-hydroxyalkanoic acids or (*R*)-3-hydroxyalkanoates is very difficult. Thus, we feel that there is a need for a new method of synthesis of biodegradable polymers analogous to that of P(3HB).



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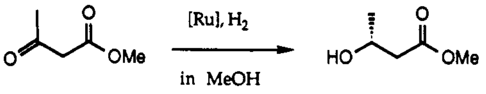
Methyl (*R*)-3-hydroxybutyrate (3HB), which is the key unit in P(3HB), and P(3HB-*co*-3HV), can economically be obtained by the asymmetric hydrogenation of methyl acetoacetate catalyzed by Ru-(*R*)-BINAP (ruthenium-(*R*)-2,2′-bis(diphenylphosphino)-1,1′-binaphthyl) complexes (eq 1).[5]



(1)

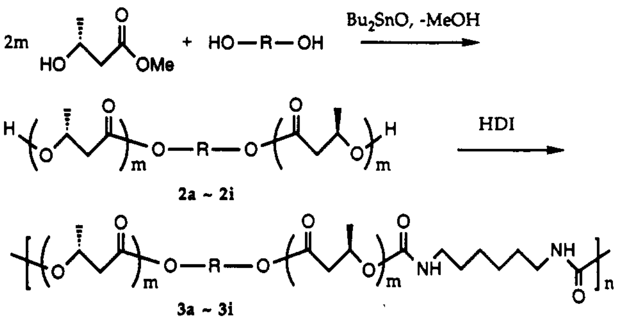
[Ru] : $Ru_2Cl_4((R)\text{-BINAP})_2 \bullet Et_3N$

This prompted us to explore chemical synthetic methods in order to prepare novel biodegradable polymers containing P(3HB) segments.

Here we report on the synthesis and biodegradability of a series of novel poly(urethane ester) compounds containing more than 67% of 3HB units (Scheme I).

Experimental Section. Methyl (*R*)-3-hydroxybutyrate (3HB), diols, and 1,6-hexamethylenediisocyanate (HDI) were dried and distilled under reduced pressure. P(3HB-*co*-3HV) was purchased from Aldrich Chemical Co. The molecular weights of the telechelic oligomers were determined by ^{1}H NMR spectroscopy. The molecular weights of the polymers were determined by GPC using a polystyrene calibration. Proton nuclear magnetic resonance spectra were recorded on a Bruker AM-400 spectrometer. Calorimetric measurements (DSC) of polymers were carried out on a Shimadzu thermal analysis system in a temperature range of −50 to +200 °C at a heating rate and a cooling rate of 10 °C/min. The melting temperature (T_m) was taken as the peak temperature of the melting endotherm (first run). The glass transition temperature (T_g) was taken as the inflection point of the specific heat increment at the glass transition (second run).

Scheme I



m : average value

	R	MW
a : m = 3, R =	$-CH_2C\equiv CCH_2-$	603
b : m = 5, R =	$-CH_2CH_2CH_2CH_2-$	951
c : m = 5, R =	$-CH_2C(CH_3)_2CH_2-$	965
d : m = 5, R =	$-CH_2CH{=}CHCH_2-$ *cis*	949
e : m = 10, R =	$-CH_2CH_2CH_2CH_2-$	1812
f : m = 10, R =	$-CH_2C(CH_3)_2CH_2-$	1826
g : m = 10, R =	$-CH_2CH{=}CHCH_2-$ *cis*	1810
h : m = 14, R =	$-CH_2CH_2CH_2CH_2-$	2501
i : m = 16, R =	$-CH_2CH_2CH_2CH_2-$	2845

General Synthesis of Telechelic Oligomers. The reaction of 3HB with 2,2-dimethyl-1,3-propanediol is a representative example.

A mixture of 3HB (105.50 g, 0.893 mol), 2,2-dimethyl-1,3-propanediol (9.30 g, 0.0893 mol), and *n*-dibutyltin oxide (Bu_2SnO) (0.74 g, 3.0 mmol) was heated in a 200-mL three-necked flask at 130 °C for 3 h under a gentle stream of nitrogen at atmospheric pressure. The reaction mixture was heated 5 h further at 140 °C while gradually reducing the pressure from 100 to 0.5 mmHg. The telechelic oligomer (**2c**; 82.8 g) was obtained in a yield of 96.1% without purification. ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.08–1.00 (m, 2,2-dimethyl-1,3-propanediol unit, $C(CH_3)_2$), 1.18–1.35 (m, 3HB unit, CCH_3), 2.34–2.70 (m, 3HB unit, CCH_2COO), 3.83–3.95 (m, 2,2-dimethyl-1,3-propanediol unit, OCH_2C), 4.12–4.23 (m, 3HB unit, OCHC terminal unit of the oligomer), 5.17–5.33 (m, 3HB unit, OCHC). Other reactions were carried out in a similar manner.

General Synthesis of Poly(urethane ester). The reaction of **2c** with HDI is a representative example.

HDI (4.20 g, 24.9 mmol) was added gradually over 3 h to the oligomer (**2c**; 24.07 g, 24.94 mmol) in a 200-mL three-necked flask while heating the reaction mixture at 110–150 °C. The reaction mixture was then heated a further 2 h. Purification of the reaction mixture from trichloromethane and hexane afforded 23.9 g (yield 84.6%) of the poly(urethane ester) (**3c**). ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.96 (s, 2,2-dimethyl-1,3-propanediol unit, $C(CH_3)_2$), 1.22–1.30 (m, 3HB unit, CCH_3), 1.32 (br, HDI unit), 1.48 (br, HDI unit), 2.40–2.70 (m, 3HB unit, CCH_2COO), 3.14 (br, HDI unit), 3.83–3.96 (m, 2,2-dimethyl-1,3-propanediol unit, OCH_2C), 4.85 (br, NH), 5.05–5.33 (m, 3HB unit, OCHC). Other reactions were carried out in a similar manner.

Biodegradation Test. Biodegradation tests of poly(urethane ester) films were carried out at 30 °C in a 500 ppm activated sludge.[6] The crude activated sludge was obtained from the sewage treatment plant at the Hira-

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Table I
Polymerization Results of Telechelic Oligomer with HDI

polymer no.	T_m, °C	T_g, °C	wt % 3HB	mol wt[a] $\bar{M}_n$	mol wt[a] $\bar{M}_w/\bar{M}_n$
3a	45	10	67	43 000	1.7
3b	78	−5	77	32 000	1.9
3c	74	1	76	40 000	1.7
3d	80	−3	77	24 000	2.0
3e	118	1	87	28 000	1.9
3f	120	4	86	22 000	2.0
3g	117	1	87	21 000	2.0
3h	134	−2	90	11 000	2.1
3i	138	5	91	15 000	1.9

[a] Determined by GPC analysis, calibrated to a polystyrene standard.

tsuka factory of Takasago International Corp., Japan. Poly(urethane ester) films (initial weights, 13.0–20.0 mg; initial film dimensions, 10 × 20 mm wide and 0.06–0.10 mm thick) were placed in 100-mL bottles. The reaction was started by the addition of 50 mL of an aqueous solution of the activated sludge and then was incubated at 30 ± 0.1 °C with shaking for 4 weeks. Samples were removed once a week, washed with water, and dried to constant weight in vacuo.

Results and Discussion. The synthesized poly(urethane ester) has three types of components: a 3HB, a diol, and a diisocyanate component, among which 3HB unit is essential for biodegradability. We prepared nine polymers (**3a–i**; Scheme I) containing various types of diols and changing the number of 3HB (m). The average value of m ranges from 3 to 16. The results are summarized in Table I. In the case of polymers **3b–d** where the average value of m is 5, the T_m and T_g values are in the range of 74–80 and −5 to +1 °C, respectively. For polymers **3e–g**, where m is 10, the T_m and T_g are in the range of 117–120 and 1–4 °C, respectively. In general, the results indicate that the T_m and T_g values are not significantly affected by the type of diol unit. However, significant changes in polymer properties were observed by changing the number of 3HB units. As the percentage of 3HB unit increases, the polymer becomes more brittle. The polymers containing 87% or more of 3HB unit were found to be very brittle.

Parts a and b of Figure 1 illustrate the relation of T_m and T_g values with 3HB percent content of polymers **3b**, **3e**, **3h**, and **3i** (all containing the same diol unit), respectively. Both T_m and T_g values are directly related to the content of the 3HB unit. Thus, by increasing the 3HB content, polymers with higher T_m and T_g values can be obtained.[7]

In the case of polymer **3a**, the T_g was found to be 10 °C which is significantly higher than all the other polymers. The reason for this is not yet known.

The biodegradability of polymers **3b–e** was assessed using solution-cast films at 30 °C in aqueous solutions of an activated sludge. It has been confirmed that no erosion occurs at 30 °C in the absence of the activated sludge. All polymers showed to have the same degree of biodegradability. Here we report the results obtained for polymer **3c** as an example.

Figure 2 shows the weight loss profiles of **3c** of P(3HB-*co*-10.88% 3HV) (M_n 198 000, M_w/M_n = 2.0) films as a function of degradation time. The average weight loss of **3c** was 12.6 mg (70%) within a 4-week period. Under the same conditions, the average weight loss of P(3HB-*co*-10.88% 3HV) was 13.4 mg (93%).

It has been disclosed that the novel poly(urethane ester) **3c** comprising P(3HB) segments was almost as biodegradable as P(3HB-*co*-10.88% 3HV) by the activated sludge.

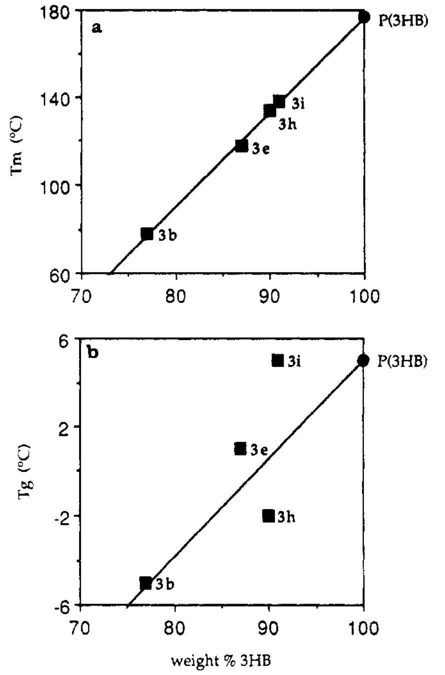

Figure 1. (a) Relation between the weight percentage of the P(3HB) segment and T_m. (b) Relation between the weight percentage of the P(3HB) segment and T_g.

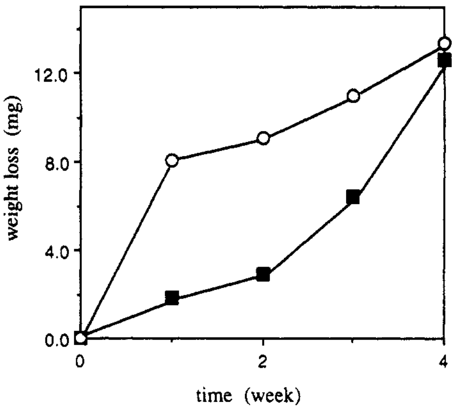

Figure 2. Biodegradation profiles on solution-cast films of **3c** and P(3HB-*co*-10.88% 3HV) samples in the aqueous solution of activated sludge at 30 °C: (■) **3c**; (○) P(3HB-*co*-10.88% 3HV).

References and Notes

(1) For reviews, see: (a) Dawes, E. A.; Senior, P. J. *Adv. Microbiol. Physiol.* **1973**, *10*, 135–266. (b) Holmes, P. A. *Developments in Crystalline Polymers-2*; Bassett, D. C., Ed.; Elsevier Applied Science: London, 1988; pp 1–65. (c) Marchessault, R. H.; Bluhm, L.; Deslandes, Y.; Kramer, G. K.; Orts, W. J.; Sundararajan, P. R.; Taylor, M. G.; Bloembergen, S.; Holden, D. A. *Makromol. Chem., Macromol. Symp.* **1988**, *19*, 235–254.

(2) Holmes, P. A. *Phys. Technol.* **1985**, *16*, 32.

(3) Doi, Y.; Kanesawa, Y.; Kunioka, M. *Macromolecules* **1990**, *23*, 26 and references cited therein.

(4) The chemical synthesis of P(3HB) by ring-opening polymerization of (*R*)- or (*S*)-β-butyrolactone is reported. (a) Shelton, J. R.; Agostini, D. E.; Lando, J. B. *J. Polym. Sci., Polym. Chem. Ed.* **1971**, *9*, 2789. (b) Zhang, Y.; Gross, R. A.; Lenz, R. W. *Macromolecules* **1990**, *23*, 3206. (c) Doi, Y.; Tanahashi, N. *Macromolecules* **1991**, *24*, 5732.

(5) Noyori, R.; Ohkuma, T.; Kitamura, M.; Takaya, H.; Sayo, N.; Kumobayashi, H.; Akutagawa, S. *J. Am. Chem. Soc.* **1987**, *109*, 5857.

(6) The test was conducted in accordance with OECD Test Guideline No. 302 and modified in accordance with the method described in the literature: Doi, Y.; Segawa, A.; Kunioka, M. *Int. J. Biol. Macromol.* **1990**, *12*, 106.

(7) The correlations of wt % 3HB with T_g and T_m are within the experimental errors.